UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/851,965	05/06/97	YOUNG A	224/042

022249
LYON & LYON LLP
SUITE 4700
633 WEST FIFTH STREET
LOS ANGELES CA 90071-2066

HM22/0712

EXAMINER	
CELSA, B	
ART UNIT	**PAPER NUMBER**
1627	14

DATE MAILED: 07/12/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

file copy

Office Action Summary

Application No.	Applicant(s)
08/851,965	Young et al.
Examiner	**Group Art Unit**
Bennett Celsa	1627

☒ Responsive to communication(s) filed on *May 17, 1999*.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1, 2, 4-10, and 13* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 2, 4-10, and 13* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *13*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Response to Amendment

Applicant's amendment and Petition to Revive dated 5/17/99 in paper no. 10 is acknowledged.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Claims

Claims 1-2, 4-10 and 13 are currently pending and under consideration.

Withdrawn Objection(s) and/or Rejection(s)

Applicant's arguments and/or amendments have overcome the Objections to the specification.

Applicant's amendment has overcome the rejection of claims 4-8 and 10-12 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 (especially patent claim 22) of U.S. Patent No. 5,677,279 in view of Ghyczy et al., . U.S. at. No. 4,528,193 (7/85).

Applicant's amendment making the claim 4 dependent on claims 1 and 2 have overcome the rejection of claims 4-8 and 10-12 under 35 U.S.C. 103(a) as being unpatentable over Young, U.S. Pat. No. 5,677,279 (10/97: filed 12/96) and Ghyczy et al., . U.S. Pat. No. 4,528,193 (7/85).

***Outstanding Objection (s) and/or Rejection* (s)**

2. Claims 1, 2, 5 and 13 are rejected under 35 U.S.C. 102(a) as being anticipated by WPIDS Abstract No. 98-019088 to Liu et al. CN 1133718 (10/96).

The Abstract discloses a pharmaceutical composition comprising amylin which when administered to a human cures gastrosis (e.g. gastritis and gastric ulcer) with a 90% total effective rate and a 50% cure rate without toxic side effects.

3. Claims 1, 2, 5, 6 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over WPIDS Abstract No. 98-019088 to Liu et al. CN 1133718 (10/96).

The Abstract discloses a pharmaceutical composition comprising amylin which when administered to a human cures gastrosis (e.g. gastritis and gastric ulcer) with a 90% total effective rate and a 50% cure rate without toxic side effects. Although, the Abstract discloses the administration, in general, of an amylin composition to cure gastrosis (e.g. prevent and/or treat) the abstract is silent as to a specific mode of administration (e.g. buccal, oral etc.). The WPIDS Abstract provides clear motivation for the skilled artisan to prepare pharmaceutical dosage formulations for administration to prevent/treat gastrosis. The making of pharmaceuticals and the determination of optimum delivery dosages and means of administration is within the skill of the art. Accordingly, the making and use of pharmaceutical dosage formulations for various modes of administration of pharmaceuticals containing amylin for treating/prevention gastrosis would have

been prima facie obvious to the skilled artisan at the time of applicant's invention in view of the WPIDS Abstract teaching..

Discussion

Applicant's arguments directed to the above anticipation and obviousness rejections over the Liu WPIDS Abstract were considered but deemed nonpersuasive for the following reasons.

Initially, it is noted that the scope of claims of the above rejections was modified to incorporate newly added claim 13.

Applicant argues that "Amylin is not a Chinese medicine" and that "Amylin" as disclosed in the Abstract may be referring to a plant extract that has been referred to in the past as "amylin".

The Examiner respectfully disagrees. The Abstract clearly discloses the use of "amylin". which appear to the Examiner to be the same "amylin" as presently claimed. Additionally, the reference clearly teaches an amylin containing composition for treating gastritis and gastric ulcer which is clearly within the scope of the presently claimed invention. Accordingly, prima facie anticipation is met by the reference teaching.

There is no scientific evidence to the contrary that the reference "amylin" in any way differs from the "amylin" currently claimed.

Accordingly, the above anticipation and obviousness rejections are hereby retained.

4. Claims 1-2, 5-8 and 13 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kolterman et al., WO 95/07098 (3/95)..

Kolterman et al. disclose the administration of "amylin" or "amylin agonists", especially "amylin agonist analogues" which are preferred (e.g. see pages 29-30) and tri-pro h-amylin which is most preferred (see tripro 25,28,29 human amylin, AKA AC-0137: See e.g. page 21 under "Summary of the Invention") for reducing gastric motility and slowing gastric emptying (e.g. See Abstract and PCT claims). In a preferred embodiment, AC-O137 is administered to humans (e.g. by placebo, infusion or by an IV bolus) over a wide range of dosages that are within the scope of the presently claimed invention. (E.g. see pages 24-25 and disclosed figures). The mode of administration (e.g. parenteral, nasal and oral: see page 42); the amounts administered (e.g. see pages 44-45) and the preferred (e.g. amylin analogues) and most preferred compounds (e.g. tri pro amylin analogues) are within the scope of the presently claimed invention. The actual administration to humans of compounds (e,g, AC-O137) in dosages within the scope of the presently claimed invention would necessarily anticipate the presently claimed invention drawn to the prevention of gastritis/ulcers. Additionally, the reference teaching of the administration of tri pro h-amylin to humans in amounts within the scope of the presently claimed invention directly anticipates and further anticipates (e.g. by immediately envisaging) the selection of the selection of the preferred h-amylin analogues disclosed in the reference due to the small list e.g. 20 or less (e.g. see page 29-30) and page 45 listing the top 7 amylin analogues or alternatively renders obvious the selection of the preferred amylin analogues for use in the disclosed method.

Accordingly, the reference method of reducing gastric motility and slowing gastric emptying (or any of the other reference methods) serves to inherently "prevent" or alternatively would be expected to prevent gastritis (or ulceration) because the *same peptide(s)* is applied in the *same way (e.g. administered in the same way to the same host)* in the *same amount. In re Best*, 195 USPQ 430,433 (CCPA 1977); *Ex parte Novitski*, 26 USPQ2d 1389 (B.P.A.I, 1993).

Discussion

Applicant's argument directed to the above anticipation rejection over the Kolterman et al. reference was considered but deemed nonpersuasive for the following reasons.

Initially, it is noted that the above scope of claims of the above rejections was modified to incorporate newly added claim 13.

Applicant argues that "gastric slowing" and "gastroprotective actions" of a number of peptides can be clearly dissociated; citing for example extendin-4 and citing the Gedulin et al., Diabetologia Vol. 40 (Suppl 1): A300, 1997).

However, the above argument is not germaine to the above anticipation rejection which is directed to the administration of a specific peptide(s) (e.g. amylin or "agonists" thereof) to a subject in amounts and by modes of administration which are clearly within the scope of the presently claimed invention. The issue is one of inherency of pharmacological effect. These issues are not addressed by the above cited document; nor is that reference document at all relevant in addressing this issue.

Applicant next argues that the Kolterman et al. Reference fails to show that the Kolterman et al. subjects were "susceptible to gastritis or gastric ulceration". Applicant further argues that Kolterman et al. does not suggest administering amylin or a non-calcitonin amylin agonist to such a patient.

However, applicant again is failing to address the crux of the above anticipation rejection e.g. whether the administration of the same pharmacological agent (e.g. amylin or "agonists" thereof) in the same amounts in the same way (e.g. the same modes of administration) as presently claimed **to any patient (e.g. the Kolterman patient)** would necessarily INHERENTLY achieve the same "preventive" effect (e.g. prevent gastritis or ulceration) as presently claimed. An affirmative answer to this question is inevitable; especially in the present instance since the reference is clearly targeting the same area of the body (e.g. the stomach) as in the presently claimed invention.

Accordingly, the above rejection is hereby retained.

5. Claims 1-2 and 5-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al., U.S. Pat. No. 4,530,838 (7/85), Gray et al, Annals of Surgery, Vol. 219 No. 1 pages 58-64, CAPLUS AN 1987:79162 to Maggi et al., Gen. Pharm. (1987) Vol. 18(1) pages 33-4 and Gheczy et al, U.S. Pat. No. 4,528,193 (7/85).

The presently claimed invention encompasses the use of "amylin agonists" which exclude calcitonin or Calcitonin Gene Related peptide (CGRP) for its gastric protective effect (e.g. treat

gastritis or gastric ulceration). The presently claimed invention includes the concomitant administration of an amylin agonist with a nonsteroidal antiinflammatory agent (combined pharmaceuticals) in order to alleviate the gastric irritation resulting from the NSAID.

The gastroprotective (e.g. against gastritis, especially ulcerative) use of CGRP and analogs (E.g. substitution analogs) thereof is known in the prior art.

For example, Evans et al., U.S. Pat. No. 4,530,838 (7/85) discloses Calcitonin Gene Related Peptide (CGRP) and an analogue thereof for lowering gastric acid secretion in mammals (including humans) upon administration (e.g. orally intranasal: e.g. see col. 9 and patent claims, especially claims 7-9).

Additionally, Gray et al, Annals of Surgery, Vol. 219 No. 1 pages 58-64 discloses the role of CGRP in protecting against gastric ulceration in a rat model (e.g. see pages 59-62 and DISCUSSION).

The use of NSAID's to treat inflammatory diseases (e.g. rheumatism) and pain and the adverse side effects thereof (e.g. stomach inflammation; e.g. ulcers) is also known in the art (e.g. see column 1 of Gheczy et al, U.S. Pat. No. 4,528,193 (7/85).

Further, the anti-ulcer activity of CGRP in rats, in general, and particularly with regard to alleviating ulcers which resulted from the administration of NSAID's (e.g. indomethacin and acetylsalicylic acid) is disclosed by CAPLUS AN 1987:79162 to Maggi et al., Gen. Pharm. (1987) Vol. 18(1) pages 33-4.

Accordingly, it would have been obvious at the time of applicant's invention to utilize an amylin agonist (e.g. CGRP OR an analog of CGRP) alone to alleviate stomach inflammation (e.g. gastritis, ulcers etc.) or concomitantly (e.g. in combined pharmaceuticals or in separate administrations) with NSAID's in order to alleviate the undesirable side effects of NSAIDS (e.g. stomach inflammation and/or ulcers), as disclosed in the above references, with a reasonable expectation of success.

6. Claims 1-2 and 5-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al., U.S. Pat. No. 4,530,838 (7/85), Gray et al, Annals of Surgery, Vol. 219 No. 1 pages 58-64, CAPLUS AN 1987:79162 to Maggi et al., Gen. Pharm. (1987) Vol. 18(1) pages 33-4 and Bates et al., Br. J. Of Pharmacology Vol. 67(3) (Nov. 1979) pages 483P-484P in view of the Specification admission as to prior art on page 6, Kolterman et al., WO 95/07098 (3/95) and WPIDS Abstract No. 98-019088 to Liu et al. CN 1133718 (10/96), taken separately or in combination.

The presently claimed invention encompasses the use of "amylin" and amylin agonists" for their gastric protective effect (e.g. treat gastritis or gastric ulceration) alone or combined with a nonsteroidal antiinflammatory agent (combined pharmaceuticals) in order to alleviate the gastric irritation resulting from the NSAID.

The gastroprotective (e.g. against gastritis, especially ulcerative) use of CGRP (an amylin agonist) and a CGRP analogue is known in the prior art. For example, Evans et al., U.S. Pat. No.

4,530,838 (7/85) discloses Calcitonin Gene Related Peptide (CGRP) and homologues thereof for lowering gastric acid secretion in mammals (including humans) upon administration (e.g. orally intranasal: e.g. see col. 9 and patent claims, especially claims 7-9).

Additionally, Gray et al, Annals of Surgery, Vol. 219 No. 1 pages 58-64 discloses the role of CGRP in protecting against gastric ulceration in a rat model (e.g. see pages 59-62 and DISCUSSION).

Further, the anti-ulcer activity of CGRP in rats, in general, and particularly with regard to alleviating ulcers which resulted from the administration of NSAID's (e.g. indomethacin and acetylsalicylic acid) is disclosed by CAPLUS AN 1987:79162 to Maggi et al., Gen. Pharm. (1987) Vol. 18(1) pages 33-4.

Similarly, Bates et al. disclose the use of a calcitonin (e.g. salmon calcitonin) for its gastroprotective effects in the prevention/treatment of indomethacin (e.g. NSAID) induced gastric ulceration in the rat. Accordingly, it would have been obvious at the time of applicant's invention to utilize an amylin agonist (e.g. calcitonin and/or CGRP) alone to alleviate stomach inflammation (e.g. gastritis, ulcers etc.) or concomitantly (e.g. in combined pharmaceuticals or in separate administrations) with NSAID's in order to alleviate the undesirable side effects of NSAIDS (e.g. stomach inflammation and/or ulcers), with a reasonable expectation of success.

However, the above references fail disclose the use of amylin or its analogues for their use for treating gastritis (or ulceration) alone or combined with NSAID's to alleviate the NSAID's side effects.

Both Amylin and amylin agonists are known to potently inhibit gastric emptying in rats, dogs and humans, especially use of the amylin agonist analogue AC187 (tri-Pro-amylin) (e.g. see specification at page 6).

Similarly, Kolterman et al. reference disclose the administration of "amylin" or "amylin agonists", especially "amylin agonist analogues" which are preferred (e.g. see pages 29-30) and tri-pro h-amylin which is most preferred (see tripro 25,28,29 human amylin, AKA AC-0137: See e.g. page 21 under "Summary of the Invention") for reducing gastric motility and slowing gastric emptying (e.g. See Abstract and PCT claims).

Accordingly, the specification admission and/or the Kolterman reference establish the *functional equivalency* between amylin, amylin agonists (e.g. calcitonin and CGRP) and amylin analogues in effecting gastric activity (e.g. gastric motility and emptying).

It is also noted that CGRP and Amylin share a high degree of homology (e.g. 50% homology).

Still further, it is noted that the WPIDS Abstract discloses a pharmaceutical composition comprising amylin which when administered to a human cures gastrosis (e.g. gastritis and gastric ulcer) with a 90% total effective rate and a 50% cure rate without toxic side effects.

Accordingly, the specification, the Kolterman reference and the WPIDS Abstract, taken separately, or in combination, teach the functional equivalency of amylin and its agonists, including amylin agonist analogues in effecting gastric functions including emptying, motility and anti-inflammation.

Thus, the skilled artisan would have a reasonable expectation to expect that amylin and its analogues (e.g. tri-Pro amylin) would act similarly to amylin analogs (e.g. calcitonin and CGRP) which were shown in the primary references to possess gastric protective activity (e.g. anti-ulcer or anti-inflammatory activity). Accordingly, it would have been prima facie obvious to the skilled artisan at the time of applicant's invention to substitute amylin and its analogues for amylin agonist (e.g. CGRP and calcitonin) to obtain pharmaceuticals containing amylin or analogues thereof for their expected use in preventing/treating gastritis or ulceration alone or combined with NSAID"S in order to alleviate the NSAID"s known side-effects (e.g. stomach inflammation, ulcers etc.) in view of the primary reference teaching of the amylin agonists use as antiulcer agents and the secondary references teachings of the functional equivalency of amylin agonists and amylin and its analogues in effecting gastric function .

Discussion

Applicant's arguments directed to the above obviousness rejections were considered but deemed nonpersuasive for the following reasons.

Applicant argues (e.g. in response to the Evans patent) that amending to exclude "a CGRP" is sufficient to overcome the above obviousness rejections.

The Examiner respectfully disagrees.

The Evans et al. reference teaches the use of CGRP and an analogue of CGRP for decreasing gastric secretion.

To the extent that applicant's claim exclusion is directed solely to disclaiming CGRP, the Evans et al. Reference teaching of an CGRP analogue is not within this exclusion.

In this regard it is noted that if the disclaimer is interpreted to cover CGRP analogues (which is CLEARLY not supported by the specification); such a limitation can be extended to also exclude amylin and its analogues which are highly homologous to CGRP.

Applicant next argues mechanism with a citation to a reference published after the filing date of the present application (e.g. Guidobono et al.: 1998) for support.

Citation of a reference AFTER the filing date of the present application to rebut obviousness, which is a determination that must be evaluated AT THE TIME OF FILING OF THE PRESENT application, is clearly not relevant.

Applicant then cites Young et al. FEBS Lett: 1997 for the premise that it is primarily amylin receptors which are responsible for the beneficial gastroprotective action.

Initially it is noted that the Examiner lacks a copy of the reference article; and is further unaware as to the publication date of the Young et al. Article and as such its relevancy.

Secondly, applicant's argument is not commensurate in scope to the presently claimed invention which broadly encompasses the use of any "amylin agonist" (with specific exclusions) and not just amylin.

Thirdly, absolute certainty is not the requirement for obviousness but only a reasonable certainty is required.

The above rejection provides evidence that amylin, CGRP (and its analogs) and calcitonin would have be reasonably expected to act as functional equivalents in the context of the presently claimed invention.

Applicant's argument and cited reference does not obviate the reasonable likelihood regarding functional equivalency of amylin, calcitonin and especially CGRP and its analogues which share a high degree of homology with amylin. .

Accordingly, the above obviousness rejections are hereby maintained.

New Objection(s) and/or Rejection(s)

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-2, 4-10 and 13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's have amended the claims to exclude by proviso "a CGRP" citing page 7, line 15 for support.

However, page 7, line 15 referring to CGRP does not provides support for a proviso excluding CGRP. To the extent that "a CGRP" extends to derivatives and/or analogues of CGRP, the specification further fails to support the exclusion of these additional species. Any negative limitation or exclusionary proviso must have basis in the original disclosure. See Ex parte Grasselli , 231 USPQ 393 (Bd. App. 1983) aff'd mem., 738 F.2d 453 (Fed. Cir. 1984) and MPEP.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-2, 4-6, 9-10 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In amended claim 1, the metes and bounds as to what compounds are excluded by use of the term "a CGRP" is not known. Just CGRP? Or Any CGRP "analogue" (including amylin or its analogues?).

11. Claims 1-2, 4, 6, 9-10 and 13 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Guidobono et al., Br. J. Pharmacology Vol. 120(4) pages 581-586 (2/97)..

Guidobono et al. (Br. J.) teach that amylin s.c/i.c.v administration in a rat prior to or subsequent to indomethacin administration protects against gastric inflammation (e.g. gastric ulcers). See e.g. abstract; pages 581-583.

12. Claims 1-2, 4-6, 9-10 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guidobono et al., Br. J. Pharmacology Vol. 120(4) pages 581-586 (2/97)

Guidobono et al. (Br. J.) teach that amylin s.c/i.c.v administration in a rat prior to or subsequent to indomethacin administration protects against gastric inflammation (e.g. gastric ulcers). See e.g. abstract; pages 581-583.

Guidobono et al. differs from the presently claimed invention (e.g. present claim 5) since the gastroprotective effect of amylin is achieved in rats and not humans as presently claimed.

However, due to the similarity between rats and humans (e.g. mammals) one of ordinary skill in the art would reasonably expect that a gastroprotective effect of amylin, as found in rats by Guidobono et al. (Br. J) would be extrapolatable to humans.

With regard to administration other than subcutaneous as taught by Guidobono et al., it is well within the skill of the art to determine and optimize amounts and means of administration.

Accordingly, the use of amylin to prevent/treat gastric inflammation (e.g. ulceration) in humans would have been obvious to one of ordinary skill in the art at the time of applicant's invention in view of the Guidobono et al. effect of amylin as found in rats.

13. Claims 1, 2, 5, 6 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guidobono et al., Peptides Vol. 15 No. 4 pages 699-702 (1994)..

Guidobono et al. (Peptides) teaches that amylin administered to rat peripherally (subcut) and intracerebroventricularly resulted in the inhibition of acid gastric secretion; and thus is gastroprotective.

Accordingly, the Guidobono et al. reference would render obvious the use of amylin to prevent/treat gastric inflammation (e.g. ulcers) which result from acid gastric secretion in rats and in humans to which the rat model is extrapolatable. The determination of additional means of administration protocols is well within the skill of the art and prima facie obvious.

14. Claims 1-2, 4-10 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Young US Pat. No. 5,677,279 (10/97), Ghyczy et al. US. Pat. No. 4,528,193, Guidobono et al., Br. J. Pharmacology and/or .Guidobono et al., Peptides in view of

Young et al. teach the administration of amylin or an agonist alone or with another pain relief agent for treating pain which is present in most inflammatory conditions (e.g. see Young et al. Col. 4, lines 55-67) and patent claims 1-22.

Ghyczy et al. discloses that nonsteroidal anti-inflammatory drugs (E.g. NSAIDS) are conventionally known as pain relief agents but may result in inflammation (e.g. stomach ulcers) and are thus preferably coadministered with gastroprotective substances (E.g. phospholipids). See e.g. Ghyczy et al. At col. 1-2.

Thus, the Young and Ghyczy et al. references would teach the combination of amylin (and its agonists) with conventional anti-inflammatory drugs (e.g. NSAIDs) for treating pain which arise from inflammation.

However, the Young et al. and Ghyczy et al. references differ from the presently claimed invention by failing to teach that amylin or its "agonists" possess gastroprotective (e.g. anti-inflammatory) properties).

Guidobono et al. (Br. J.) teach that amylin s.c/i.c.v administration in a rat prior to or subsequent to indomethacin administration protects against gastric inflammation (e.g. gastric ulcers). See e.g. abstract; pages 581-583.

Additionally, Guidobono et al. (Peptides) teaches that amylin administered to rat peripherally (subcut) and intracerebroventricularly resulted in the inhibition of acid gastric secretion; and thus is gastroprotective.

Accordingly, either Guidobono et al. reference taken separately or in combination would teach that amylin and its agonists would be expected to be gastroprotective in mammals (e.g. rats/humans).

The making of pharmaceuticals and determining optimum delivery modalities is well within the skill of the art.

Accordingly, it would have been obvious to administer amylin (and its analogs) alone or in conjunction with an NSAID agent since the Guidobono et al. References teach and suggest the use of amylin (and its analogs) for gastroprotection in response to NSAID administration for pain

relief; and further in view of the benefits of getting increased pain relief due to co- or sequential administration of amylin and pain relief agents as suggested by the Young US Pat. No. 5,677,279 (10/97) and Ghyczy et al. references.

15. Applicant's submission of an information disclosure statement under 37 CFR 1.97© with the fee set forth in 37 CFR 1.17(p) on 8/4/99 and Amended Claims prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609(B)(2)(I). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

General information regarding further correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Celsa whose telephone number is (703) 305-7556.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat (art unit 1627), can be reached at (703)308-0570.

Any inquiry of a general nature, or relating to the status of this application, should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Bennett Celsa (art unit 1627)

July 10, 2000

BENNETT CELSA
PRIMARY EXAMINER